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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,413	08/27/2003	Axel Ullrich	224160	5257

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EXAMINER	
SHAFER, SHULAMITH H	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,413	ULLRICH ET AL.	
	Examiner	Art Unit	
	Shulamith H. Shafer, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,7 and 11-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,7,11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/7/06,9/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Status of Application, Amendments, And/Or Claims

The amendment received 7 August 2006 in response to the Office Action of 1 May 2006 has been entered. Claims 2, 5, 6, 8-10, 14-29 have been cancelled. Claims 1, 3, 7, 11, and 13 have been amended and the amendments have been entered. Claims 1, 3, 4, 7, 11-13 are pending. The pertinent remarks/arguments filed with the amendment received 7 August 2006 will be responded to herein.

The text of those sections of Title 35 U.S. Code not included in this action can be found in the prior Office action.

Objections/Rejections Withdrawn

Withdrawn Objections:

The objection to the specification is withdrawn in view of applicants' amendment to the specification indicating parent application has issued as U.S. 6,770,742.

The objection to the IDS is withdrawn in view applicants' submission of references. Only the English translation of the abstract of reference AQ was submitted to the Office; therefore, only the abstract has been considered by the examiner.

Withdrawn Rejections:

The rejection of claims 1, 3, 4, 7, and 11-13 under U.S.C. 112, second paragraph, as set forth in the Office Action of 1 May 2006, as being vague and indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's amendments to the claims.

The rejection of Claims 1, 3, 4, 7, and 11-13 under 35 U.S.C. 112, first paragraph, as set forth in the Office Action of 1 May 2006, because the specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims is withdrawn in view of applicants' amendments to the claims.

The rejection of Claims 1, 3, 4, 7, and 11-13 under 35 U.S.C. 112, first paragraph, as set forth in the Office Action of 1 May 2006, as failing to comply with the written description requirement is withdrawn in view of applicants' amendments to the claims.

The rejection of Claims 1 and 3 under 35 U.S.C. § 102(b) as being anticipated by Takahashi et al. (1991, FEBS 288:65-71) is withdrawn in view of applicants' amendments to the claims.

Maintained/New Rejections

35 U.S.C. § 112, Second Paragraph

Claims 1, 3, 4, 7, and 11-13 are rejected under 35 U.S.C., second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to read (at line 3-4) wherein (i) the mammal comprises a mutated fibroblast growth factor receptor-4 (FGFR-4) protein..... It is unclear, from the claim as presented, if applicant intends the mammal to be a transgenic animal engineered to express the mutated FGFR-4 protein, or the mammal has an endogenous mutated FGFR-4 protein. Furthermore, there is no nexus in the claim, as presented, between the cancer and the mutated FGFR-4 protein.

Claims 3, 4, 7, and 11-13 are included in this rejection as being dependent upon a rejected claim.

35 U.S.C. § 112, First Paragraph

Claims 1, 3, 4, 7, 11-13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for a method for the therapeutic treatment of a cancer wherein the cancer is breast cancer, and wherein the

mammal comprises a mutated fibroblast growth factor receptor-4 protein wherein the mutation is in the transmembrane domain of FGFR-4 protein at position 388 in which a glycine amino acid is substituted for an arginine amino acid, the sequence of which is deposited in the EMBL Gene Bank/DDBJ under X57205 does not reasonably provide enablement for a method for the therapeutic treatment of any cancer wherein the mammal comprises a mutated fibroblast growth factor receptor-4 protein wherein the mutated FGFR-4 protein comprises at least one point mutation in the transmembrane domain of FGFR-4 that substitutes a hydrophilic amino acid for a hydrophobic amino acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)).

Breadth of the claims: Claim 1, the independent claim of the instant invention, is broadly drawn to a method for the treatment of any cancer in a mammal comprising any mutation in the transmembrane domain of a FGFR-4 receptor that substitutes a hydrophilic amino acid for a hydrophobic amino acid.

Direction/guidance in the specification: The specification discloses a correlation between expression of the mutated FGFR-4 receptor protein, the

mutation being a point mutation in the amino acid 388 wherein glycine is replaced by arginine, and increased incidence of lymph metastases and decreased relapse-free survival time in patients suffering from breast cancer.

Working examples: There are no working or prophetic examples drawn to treatment of any mammal by the methods of the instant invention.

State of the art: Streit et al. (2006. Br J of Cancer 94:1879-1886, abstract) teach that there is no correlation of the FGFR4 Arg388 allele with overall and disease-free survival in melanoma patients. Mawrin et al (2006. Cancer Letters. 239:239-245, abstract) teach that the FGFR4 Arg 388 does not play a major role in malignant gliomas.

Thus, one of skill in the art would be unable to predict that the method of the instant invention would be able to treat any cancer, or even any cancer expressing the mutated protein. Undue experimentation would be required to determine which cancers, including which ones comprising the FGFR4 mutated protein could be treated by the methods of the claimed invention.

Applicant traverses the rejection as applied to the recitation of mutated FGFR-4 receptor wherein the mutation comprises "at least one point mutation in the transmembrane domain of FGFR-4 that substitutes a hydrophilic amino acid for a hydrophobic amino acid". The grounds for the traversal are that the amino acid sequence of the transmembrane domain of FGFR-4 was known in the art at the time the subject application was filed, and is disclosed in the specification as SEQ ID NO:2 (page 9, paragraph 2 of Reply to Office Action of 7 August 2006) and that any experimentation required to practice the invention defined by claim 1 would be routine, not undue. Applicant's arguments have been fully considered but are not found to be persuasive for the following reasons. Applicant has taught only one specific mutation, the FGFR4 Arg 388, that is associated with increased incidence of lymph metastases and decreased relapse-free survival time in patients suffering from breast cancer. The art teaches that this mutation is not associated with poor prognosis in other forms of cancer. Therefore, even though the transmembrane domain of the FGFR4

receptor comprises a defined number of hydrophobic amino acid residues, the skilled artisan would be unable to predict which mutations or substitutions, if any, would result in a mutated FGFR4 receptor that would be associated with poor prognosis in any form of cancer. Thus, undue experimentation would be required to first generate the appropriate mutations in the transmembrane domain of the FGFR-4 receptor and then determine if said mutations are associated with poor outcome in any type of cancer.

Due to the large quantity of experimentation necessary to determine which cancers, other than breast cancer comprising the specific FGFR-4 mutation wherein the mutation comprises a point mutation in the amino acid 388 wherein glycine is replaced by arginine, could be treated by the methods of the instant invention, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to same, the breadth of the claims, which are drawn to treatment of any cancer comprising any point mutation in the FGFR-4 transmembrane domain that substitutes a hydrophilic amino acid for a hydrophobic amino acid, the complex nature of the invention, the state of the art which fails to establish a correlation between the presence of any FGFR-4 mutated protein comprising any point mutation in the FGFR-4 transmembrane domain that substitutes a hydrophilic amino acid for a hydrophobic amino acid and poor prognosis in all types of cancers, and the lack of predictability for treatment of all types of cancers, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion:

Since new grounds for rejection have been raised, this action is made non-final. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shulamith H. Shafer, Ph.D. whose telephone number is 571-272-3332. The examiner can normally be reached on Monday through Friday, 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SHS

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER